UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,003	03/22/2001	David M. Sabatini	WIBL-P02-001	5682

21559 7590 04/20/2005

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,003	SABATINI, DAVID M.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *160-177 and 237-240* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *160-177 and 237-240* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 02/10/05 has been acknowledged.

Claims 1-159 and 178-236 are canceled.

Claims 237-240 are newly filed.

Claims 160-177 and 237-240 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **571-273-8300.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

The terminal disclaimer filed on 11/24/04 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of US 6,544,790 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 102

Claims 160-175 and 237-240 are rejected under 35 U.S.C. 102(e) as being anticipated by Taylor et al (US 6,103,479 2000).

The instant claims are drawn to an array of transfected eukaryotic cells comprising a surface having an array of at least 100-1000,000 locations per square

centimeter (as claimed), wherein each location comprises eukaryotic cells that are transfected with one or more defined nucleic acid molecules.

Taylor teaches making of miniaturizes high-throughput cell array and an apparatus for cell-based screening. Regarding claims 160, 168-175 the cited art teaches a 20mmx30mm micro-patterned array of cells that fills a 1000x1500 arrays (col.16 lines 44-50). The cited art further teaches that the preferred cell types for the micro-patterned array include lymphocytes, cancer cells, fibroblasts, neurons, fungi, bacteria and other prokaryotic and eukaryotic cells (col.13 lines 5-35). The cited art further teaches micro-patterns at discrete locations comprises array of different forms, which accommodate a sample size from 1 nanoliter (nl) to 1000nl (col.9 lines 7-10). The cited art further teaches that the size of a well on micro-patterned array ranges from 200 μm to 400μm (Fig 3.B). Regarding claims 161-164 and 166-167 the cited art teaches that the cells attaches to the wells can be modified with luminescent of cell chemical or molecular properties. The indicators can be introduced into the cells before or after the cells were seeded onto array by any one or combination of variety of physical methods such as diffusion across the cell membrane, mechanical perturbation of cell membrane or genetic engineering so that they express under prescribed conditions. The cited art further teaches the use of reporter genes which encodes chemiluminescent proteins, which permits the analysis of the physiological state of cells when contacted with drugs or other reactive substances (Col.12 lines 44-67, col. 13, line 1-4). Regarding claim 165 the cited art teaches that the cells suspended in culture media at concentration from about 10^3-10^7 cells per ml are incubated in contact with the wells. The cited art teaches

that the density of cells attached to wells is controlled by the cell density in the cell suspension, time permitted for cell attachment to the well surface (col.12, lines 13-36). Thus given the broadest reasonable interpretation the cited art clearly teaches an array of transfected eukaryotic cells as claimed.

Response to Arguments

Applicant's arguments filed on pages 7 regarding prior art issues have been fully considered but they are not persuasive. The applicant argues that the claims as now amended require that the array have at least 96 locatiops at a density of at least 100 locations per square centimeter. The applicant argues that the Taylor fails to describe an array of at least 96 locations of transfected eukaryotic cells having a density of at least 100 locations per square centimeter.

However, applicant's argumetns are found NOT persuasive because Taylor clealry teacehs making of miniaturizes high-throughput cell array and an apparatus for cell-based screening, wherein a 20mmx30mm micro-patterned support fills 1000x1500 arrays which is well with the reach of location density claimed in the instant application (see col.16 lines 44-50). For example at such a density the prior art teaches accommodating at least $2.5x10^5$ locations pre square centimeter, which is about 2500 times more locations per square centimeter when compared to instant invention. The cited art further teaches that by selecting an array density, at reduced array size, not only improves the speed and efficiency of scanning for high-content screening, but also allows high throughput screening to be carried out on the same cell array by reading the whole area of the array at lower spatial resolution (col.6 lines 3-29). Thus given the

broadest reasonable interpretation the cited art clearly teaches an array of transfected eukaryotic cells as claimed.

Claim Rejections - 35 USC § 103

Claim 176 and 177 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al (US 6103,479 2000) as applied to claims 160-175 above, and further in view of Montgomery et al (Proc Natl Acad Sci U S A. 95(26): 15502-7, 1998).

Taylor et al is relied upon as described in rejection above. However, Taylor does not teach the use double-stranded RNA molecule or nucleic acid molecule having a modified base or backbone.

Montgomery teaches the double-stranded RNA mediated genetic interference in C.elegans. Regarding claim 176 the cited art teaches a nucleic acid molecule, which encodes double-stranded RNA for RNAi experiments (page 15502, col2. para.2). Regarding claim 177 the cited art teaches gene-specific probes for insitu hybridization, wherein the probe comprises Digoxigenin (DIG)-labeled single stranded DNA probe (page 15503, col.2, para. 3).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of Taylor by substituting the nucleic acid molecules with a double-stranded RNA molecule or a nucleic acid molecule having a modified base or backbone. One would have been motivated to incorporate a double-stranded RNA molecule to inhibit the expression of a gene of interest. One would have been motivated

to use a nucleic acid molecule as probe to analyze the gene expression of interest. One would have reasonable expectation of success, since transduction of eukaryotic cells with nucleic acid molecules has been routine in the art at the time of filing. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Response to Arguments

Applicant's arguments filed on pages 8-10 regarding prior art issues have been fully considered but they are not persuasive. The applicant argues that Taylor does not describe an array of at least 96 locations of transfected eukaryotic cells having a density of at least 100 locations per square centimeter and Montgomery does not remedy this deficiency. The applicant furhter argues that the in situ hybridization protocol in which chemically fixed and permeabilized cells are contacted with a digoxigenin-labeled nucleic acid is simply is not the same as transfection of a cell with a modified nucleic acid molecule. The applicant furhter argues that the nothing in either Taylor or Montgomery provides any motivation for one skilled in the art to substitute Montgomery's double-stranded RNA or digoxigenin-labeled nucleic acid or Taylor's reporter genes.

However, applicant's argumetns are found NOT persuasive. As stated above Taylor clealry anticipate location density of 100 locations per square centimeter. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references

themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law (See MPEP 2144). In this case, the Taylor clearly teaches a micro array comprising of location greater than 96 locations at the density of 100 locations per square centimeter (supra). Since Taylor teaches modification of cell by genetic engineering, it would have been obvious to substitute the nucleic acid molecules with a double-stranded RNA molecule or a nucleic acid molecule having a modified base or backbone in view Montgomery. Furthermore the invention as claimed herein is only limited to transfection of cells wherein the expression of transduced gene is not required. Thus combined teaching of cited art clearly suggests the delivery of double-stranded RNA molecule or a nucleic acid molecule having a modified base or backbone. In addition the arguments taken as a whole rely heavily on the deficiencies of each reference taken alone. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Thus the invention as claimed is *prima facie* obvious in view combined teaching of cited prior art of record.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

Sumesh Kaushal
Examiner GAU 1636

SUMESH KAUSHAL
PATENT EXAMINER